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A REVIEW ARTICLE ON INFLUENZA VIRUS

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ABSTRACT

Influenza Viruses, negative strand RNA viruses, belonging to *Orthomyxoviridae* family cause both seasonal and periodic respiratory infections. According to the World Health organization, Influenza virus is the major public health concern that is emerging as the pandemic diseases. It causes significant number of morbidly and mortality cases in human and birds by inducing the acute inflammation in respiratory epithelium. Influenza virus is highly contagious disease that cause symptoms ranges from fever, bodyache, fatigue and running nose. After a typical course duration of 5 to 10 days, influenza virus can also attack the lungs, brain and heart. Pregnant women, people with weak immune system, chronic respiratory diseases, infants and elder people are at the major risk of suffering from the influenza virus disease. Antiviral drugs treatment, vaccination, hospitalization are treatment and preventive strategies that can be used for the treatment of patients suffering with the influenza infection. In this article, we review the various aspects of diseases such as epidemiology, pathogenesis, signs and symptoms and treatment strategies.

KEYWORDS: Influenza, pandemic, epithelium.

INTRODUCTION

Influenza is an acute respiratory illness characterized by various symptoms such as fever, muscle pain, headache, nasal stiffness and throat pain. Various other complications such as acute injury to the lungs, increased lungs extracellular permeability due to rise in pulmonary microvascular leakage and circulatory collapse may occur in patients with weak immunity system or in elder patients. Various host and viral factors contribute to the severity and clinical outcomes of the symptoms and clinical complications of the disease.

Seasonal influenza effect atleast 40% of the population in some countries and worldwide around 500 million people die each year. Firstly, the epidemics of the influenza virus was in March, 1918 in America with mild symptoms. At least 20 million people worldwide died from virus epidemics and 675,000 people death occur in America. Majorly, people between age of 21 to 29 years died from virus epidemics.

Influenza virus, RNA enveloped virus is the major causative agent of the Influenza infection. Influenza A, B and C are the various subtypes of Influenza virus that are responsible to cause the infection in multiple species including humans, birds and swines. 1 to 4 days is the incubation period of the Influenza virus. Influenza virus is highly contagious disease that is transmitted from an infected person to other person by various ways, mostly by respiratory droplet transmission and occasionally from fomites or animals.

Immunofluroscent assay, virus cell isolation, are the currently available diagnostic techniques that can be used for the diagnosis of the Influenza Virus infection. Early diagnosis of the virus concentration in the body is important to prevent the community spread of virus infection. Rise in the level of antibodies gives confirmation of presence of influenza virus antigenic material in the patients.

Inactivated or live-attenuated vaccines are the licensesd influenza vaccines available for the treatment of type A or B viruses subtypes. Initation of treatment with the antiviral medications as soon after the illness outbreak is the need of hour. Neuramindase inhibitors, cap-dependent endonuclease inhibitors are the currently available FDA approved drugs that are used for the treatment of Influenza virus infection. These antiviral drugs are very effective in killing the RNA component of the virus.

Epidemiology

Seasonal influenza outbreak occur as a result of the variation in the antigenic properties of the glycoprotein (hemagglutinin and neuraminidase) present on the virus

surface. 90% of the morbidity and mortality cases of influenza significantly occur in the older patients. Various factors increasing the suspectibity of old age patients to infection are low cell mediated immunity, decline in muscles contraction strength of respiratory system, and presence of other abnormal medical conditions and nutritional deficiencies.

Influenza flu pandemics occur with variable intensity and extension every year. This variation in the epidemiological pattern of Influenza is due to no. of factors such as transmission potential of virus, vulnerability of population towards infection and change in antigenic shift of the virus. Out of all the strains of influenza virus, Influenza virus A strain has the significant potential to undergo variations in the antigenic properties of proteins (glycoprotein, hemagglutinin, and neuraminidase) present on its surface. "Antigenic drifts" and "Antigenic shifts " are the terms use for the characterization of changes in the antigenic properties of proteins of the virus where antigenic drift characterized minor changes and antigenic shifts is the term used for the major changes. Pandemics and epidemics outbreak of Influenza virus A occur due to antigenic shift properties of virus, while localized outbreak occur due to antigenic drifts. However, further epidemiological analysis of 1918 influenza A provide evidence that influenza pandemics occur less frequently due to major protein structure variations (antigenic shift). 1918 influenza pandemics A is characterized by a shift in the mortality from the older patients to young and healthy adults between 18 to 35 years old.

A similar such shift in the age related mortality is suggested by the preliminary data collected from the 2009 H1N1 influenza pandemics. Data collected from 532 cases reported in US in 2009 pandemic H1N1 influenza provide evidence that 60% of cases occurred in patients older than 18 years of age

Types
Influenza viruses are negative-strand RNA enveloped viruses belonging to the family *Orthomyx-oviridae.* Various types of Influenza viruses differ in their host suspectibity and their antigenic characteristics. Influenza virus are divided into three main subtypes: A, B, and C. Types A and B are responsible for most of the outburst and epidemics of Influenza virus and generally mild upper respiratory symptoms are caused by the type C.
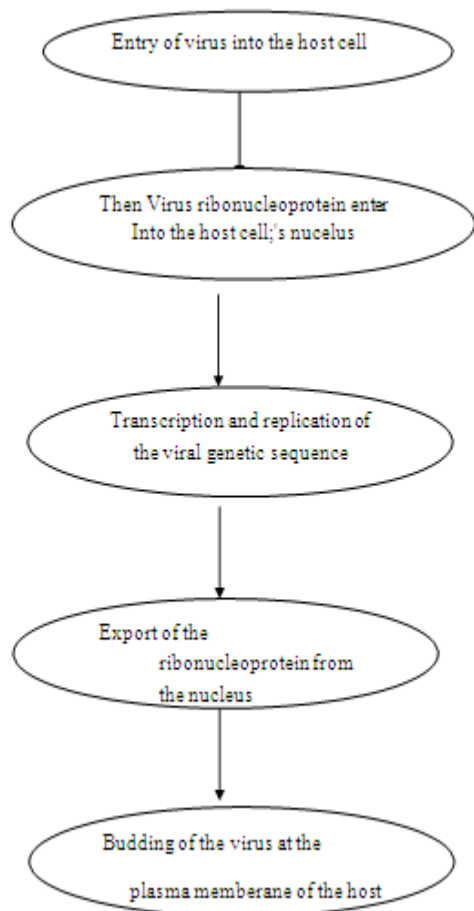
Structurally, virus are spherical and filamentous in shape with two major glycoprotein named neuraminidase and hemaglutinin over the outer layer. Both of these glycoprotein present on the virus surface play major role in the antigenicity or pathogenesis of disease.

Structure of virus
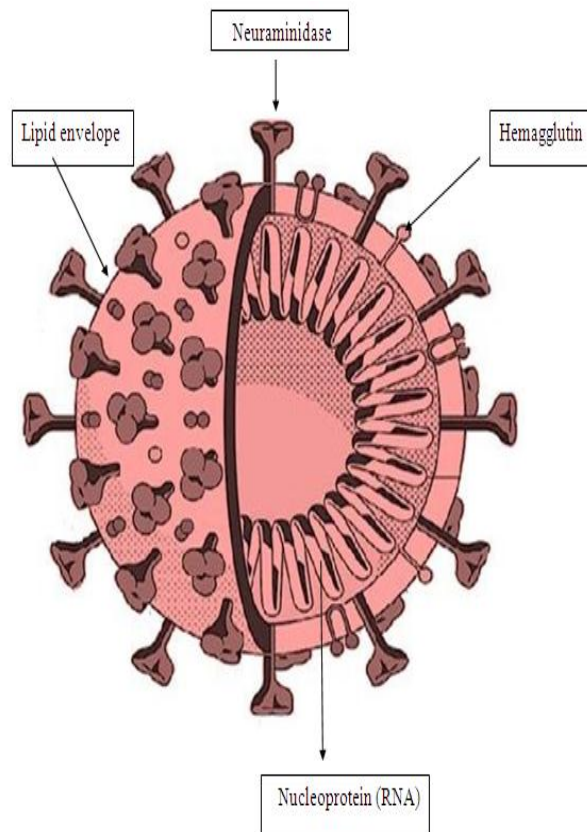
Pathogenesis
The potential of the influenza virus to induce infection is dependent on the both host and viral factors such as functioning of the virus proteins, virus capability to sustain in the environment, host innate and acquired immune response of patient body to the virus. After virus get enter into the host body by inhalation, it attaches to the columnar epithelial cells present on the respiratory track through its surface protein hemaggtutinin. Host body immune defense responses such as secretion of IgA antibodies, mucociliary clearance remove certain virus particles. However, infection continues with same intensity in older patients and smokers due to impairment of mucociliary clearance in smokers and decline secretion of IgA antibodies in older patients. Viral replication occurs due to invasion of respiratory epithelial cells. Newer replicated virus particles can cause host cell death by altering the synthesis of critical proteins and inducing the infection to large number of epithelial cells.

Entry of virus into the host cell

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Then Virus ribonucleoprotein enter Into the host cell;'s nucelus

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Transcription and replication of the viral genetic sequence

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Export of the ribonucleoprotein from the nucleus

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Budding of the virus at the plasma memberane of the host

Life cycle of the Influenza virus
Transmission
The predominant route of entry of Influenza virus in the human body is the respiratory track, mouth and nose. When an infected person cough, sneeze or talk, virus released from his body Broadly, the route of transmission of Influenza virus are divided into three categories-
1. Aerosol transmission- by inhalation of virus loaded aerosols
2. Direct contact- direct contact with infected person e.g handshake with an infected person
3. Indirect contact- in contact with contaminated objects such as toys, towels)

A number of factors are essentially required for a virus to cause infections in host body. These factors are : (a) virus must be able to survive in the environment (b) virus must reach to the target epithelial cells in the new host body (c) enough concentration of virus must be present in the target cells. The epidemics of seasonal influenza increases significantly in the late autumn and start decreasing in the month of mild spring. There is no any evidence that suggested the reason of seasonality of Influenza virus. As large droplet transmission is the primary route of transmission of Influenza virus, beginning of military recruit courses, large crowding in the colder months have been suggested as other contributing factors.

Risk Factors
Influenza is a very serious disease that can affect the millions of people. But the people with other disease such as: cardiovascular diseases, severe kidney disease, chronic obstructive pulmonary disease, asthma. diabetes, severe anaemia, various other conditions which weekend the system like treatment with steroids, chemotherapy, diseases such as HIV, AIDS. Other than this people living in the area of cold temperature and low relative humidity are more susceptible to get infected from influenza virus. It is suggested by National Institute of health that various groups of people are at the higher risk of infections from the influenza virus. These groups include:
1. Very young and old people
2. Pregnant woman
3. People with the underlying other medical conditions as described above

Various other factors such as farming practices, marketing practices (bird market), virus presence in the wild birds. Avain Influenza viruses can reside in the respiratory or intestinal track of some of the wild birds. Various protective measures have been taken around the world for the monitoring of the characteristics of the Avain Influenza virus in wild birds.

Clinical sign and symptoms
In the mild influenza infection, ruffled feather, declined production of eggs and moderate effect on the respiratory system are observed. While in the severe form of the disease, massive internal bleeding can occur due to potential of virus migration into other organs and tissues. Onset of symptoms usually begins after an incubation period of 1 to 2 days. The most prominent symptoms in the classical influenza infections are severe muscles pain, loss of apetitite and sensation of fever. Various other symptoms such as rhinorrhea, dry cough, nasal discharge and pain in throat can also occur. Various complication such as pneumonia, primary influenza viral pneumonia, secondary bacterial pneumonia can occur in the patient

Diagnosis
Nucleic acid amplification test, virus cell isolation, direct fluroscent assay(DFA) are the diagnostic techniques that have been used for the diagnosis of influenza virus detection. Since the 1960, DFA, an antigen based immunoassay is used for the diagnosis of influenza virus infection on the routine basis. It is most popularly diagnostic approach used for the diagnosis of Influenza virus detection due to its rapid advantages such as short trunaround time and simplicity involved. In this method, firstly respiratory cells are derived from nasopharyngeal swabs or nasopharyngeal aspirates of patient, then direct staining of these cells are carried out with the fluorescently labelled influenza virus-specific antibodies and lastly examination of these cells are carried out under the microscope. Further, culturing of virus cell lines is considered one of the golden approach method for the detection of the virus infections since 1940. This

diagnostic test involves the infectious sample with the embryonated eggs, then monitor the development of cytopathogenic effect by propagation it for 7-10 days and finally confirmation of infection is achieved by specific antibody staining,

Treatment and preventive strategies

Initation of treatment with the anti-viral drugs for influenza infection should be initiated as current recommendation by the local and national public health agencies. Neuramindase inhibitors, endonuclease inhibitors, and adamantases are antiviral medication approved by FDA against the influenza A and B viruses. Out of these antiviral drugs, influenza A and B virus exhibit significant resistance against the adamantases due to which they are not currently being used. Oseltamivir, zanamivir, and peramivir are the neuramindase inhibitors drugs approved by the U.S food and drug administration for the treatment of Influenza virus infection. These drugs work by the inhibiting the progession of virus by inhibiting the neuraminidase enzyme, which require for the release of progeny virions.

Several preventive measures such as ventilation of crowded places, hygienic measures, regular hand wash, can be adopted to reduce the risk of influenza infection. Vaccination is one of another best protective measure that can be used for the prevention of influenza virus infection. Currently marketed influenza vaccines work by generation of antibodies against the viral HA protein.

CONCLUSION

Influenza infection outbreak poses a significant medical problem for the group of patients at high risk including elderly and pregnant ladies. However, young adults can also effect severely by the Influenza virus infections. The rapid and continuous variations in the Influenza virus structure brings difficulty in the treatment strategies. Further, influenza virus exhibit high resistance against the adamantases and neuraminidase prescribed for its treatment. Vaccination is the best prevention strategy in the patients at high risk of influenza virus infections. A complete understanding of the pathogenesis of the influenza virus infections may help to new look at the antiviral chemoprophylaxis and may also help in the reduction of the mortality and morbidity cases with influenza virus infections.

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